DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
9 1935d

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3145

November 8, 2001

Ref: 2002-DAL-WL-04

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Thomas J. Maloney, President
Iso-Tex Diagnostics, Inc.
P.O. Box 909
1511 County Road 129
Friendswood, Texas 77546

Dear Mr. Maloney:

During an inspection of your drug manufacturing facility in Friendswood, Texas, on October 2 through 4, 2001, our investigators determined that your firm manufactures sterile radiopharmaceuticals, such as Glofil (Sodium Iothalamate I-125 Injection, USP), Megatope/Volumex (Iodinated I-131 Albumin Injection, USP), and Jeanatope (Iodinated I-125 Albumin Injection, USP). These products are drugs as defined in Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

During the inspection, our investigators documented significant deviations from the Current Good Manufacturing Practice for Finished Pharmaceuticals – Title 21, Code of Federal Regulations (CFR), Parts 210 and 211 (CGMP's). These deviations cause your drug products to be adulterated within the meaning of Section 501(a)(2)(B) of the Act. A drug is adulterated if the methods used in, or the facilites or controls used for, its manufacture, processing, packing, or holding do not conform to or are not operated or administered in conformity with current good manufacturing practices.

At the conclusion of the inspection, the investigators issued a list of Inspectional Observations (Form FDA-483) listing significant deviations from CGMP's as follows:

1. Failure to follow appropriate written procedures and conduct adequate validation of the sterilization process designed to prevent microbial contamination in drug products purporting to be sterile [21 CFR 211.113(b)]. For example, your firm:

   (a) has not performed validation of the autoclave cycles used to sterilize equipment and supplies used in the aseptic manufacture and fill of Megatope and Jeanatope [FDA-483 Item 1]; and

   (b) fails to follow the environmental control procedure (SOP# 3001, dated 4/20/00) in that monitoring of non-viable particulates has not been performed in the manufacturing and filling rooms for Glofil, Megatope, and Jeanatope [FDA-483 Item 2].

2. Failure to provide equipment for adequate control over air pressure, micro-organisms, dust, humidity, and temperature when appropriate for the manufacture, processing, packing or holding of a drug product [21 CFR 211.46(b)]. For example, the manufacturing and filling rooms of (a) Glofil, Megatope, and Jeanatope are not equipped with differential pressure monitors; and (b) Megatope and Jeanatope are not equipped with temperature and humidity control monitors [FDA-483 Item 4].

3. Failure to conduct appropriate stability testing and maintain testing records to assure a drug product meets applicable standards of identity, strength, quality, and purity at the time of use [21 CFR 211.137(a) and 21 CFR 211.194(e)]. For example, stability studies have not been performed and stability testing records have not been kept to support the expiration dates used for Megatope and Jeanatope [FDA-483 Item 6].

4. Failure to test an adequate number of batches of each drug to determine an appropriate expiration date [21 CFR 211.166(b)]. For example, only one lot of Glofil has been placed into a stability study in order to support the expiration date used [FDA-483 Item 7].

5. Failure to maintain written records of annual product reviews for each drug product [21 CFR 211.180(e)]. For example, your firm has no documentation to show that annual product reviews have been performed for Glofil, Megatope, and Jeanatope [FDA-483 Item 8].

6. Failure to maintain complaint handling procedures to include provisions for review to determine whether the complaint represents a serious and unexpected adverse drug experience which is required to be reported to FDA [21 CFR 211.198(a)] [FDA-483 Item 10].

With regard to the air filtration system, your firm was cited for not providing HEPA-filtered air into the [redacted] clean rooms as required by 21 CFR 211.46(c) Ventilation, Air Filtration, Air Heating and Cooling [FDA-483 Item 3]. You disagreed with the investigator's observation in that HEPA-filtered air is not necessary for each of the [redacted] clean rooms (Class [redacted] because the aseptic processing is being performed under the biological hoods that are equipped with HEPA filters. Your justification is not adequate because you have not provided supporting documentation of (1) air cleanliness qualification data; (2) data from a routine environmental monitoring program; (3) the specific ratings of each of the successive filters found in the HVAC system that serve the Class [redacted] clean room; and (4) diagrams/charts of the HVAC system.

Your firm was also cited for not establishing written procedures for postmarketing reporting of adverse drug experiences [FDA-483 Item 9]. Effective April 6, 1998, written procedures for the surveillance, receipt, evaluation, and reporting of postmarketing adverse drug experiences to FDA for marketed prescription drugs subject to approved applications became a requirement under 21 CFR 314.80(b). These procedures also became a requirement for drugs without approved applications under 21 CFR 310.305(a), also effective April 6, 1998.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Current Good Manufacturing Practice Regulations. Federal agencies are advised of the issuance of this Warning Letter so that they may take this information into account when considering the award of contracts. Additionally, NDA, ANDA, or export approval requests may not be approved until the above deviations are corrected.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. Possible actions include seizure and/or injunction.

Please provide this office in writing within 15 working days of receipt of this letter a report of the specific steps you have taken or will take to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be completed. Please direct your response to Thao Ta, Compliance Officer, at the above letterhead address.

Sincerely,

Michael A. Chappell
Dallas District Director

MAC:txt